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Exploring the Impact of Hypothyroidism on Renal Function: A Comparative Study of Overt and Subclinical Cases

Original Research Article

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Abstract: ***Hypothyroidism, a common endocrine disorder characterized by insufficient thyroid hormone production, has wide-ranging systemic effects. While its impact on cardiovascular and musculoskeletal systems is well-documented, the effects on renal function are less understood. Thyroid hormones play a crucial role in kidney development and function, influencing renal blood flow, glomerular filtration rate, and electrolyte homeostasis. This study aimed to assess the impact of hypothyroidism on renal function parameters and compare these effects between overt and subclinical hypothyroidism. Present cross-sectional study was conducted including 150 hypothyroid patients (56 overt, 94 subclinical) at Gandhi Medical College and Hamidia Hospital, Bhopal, over 18 months. Serum creatinine, creatinine clearance, and microalbuminuria were measured alongside thyroid function tests. Present results revealed significantly higher serum creatinine levels and lower creatinine clearance in overt hypothyroidism compared to subclinical hypothyroidism. Microalbuminuria was more prevalent in overt hypothyroidism. The results observed a positive correlation between serum TSH and creatinine, while T_4 showed a negative correlation with creatinine. These findings demonstrate a significant impact of hypothyroidism on renal function, with more pronounced effects in overt hypothyroidism. The study suggests that thyroid dysfunction, particularly overt hypothyroidism, is associated with impaired renal function as indicated by increased serum creatinine, decreased creatinine clearance, and a higher prevalence of microalbuminuria. These results underscore the importance of monitoring renal function in hypothyroid patients, especially those with overt disease. Further research is needed to elucidate the mechanisms underlying these thyroid-kidney interactions and to develop targeted strategies for managing renal complications in hypothyroid patients.***

Keywords: Hypothyroidism, overt hypothyroidism, subclinical hypothyroidism, thyroid-kidney interaction, renal function, serum creatinine, creatinine clearance, microalbuminuria

1.Introduction

The intricate interplay between endocrine systems and organ functions has long fascinated medical researchers, with the thyroid-kidney axis emerging as a particularly compelling area of study[1]. Hypothyroidism, a condition characterized by insufficient thyroid hormone production, affects millions worldwide and has far-reaching consequences beyond its well-documented impacts on metabolism and cardiovascular health[2,3]. In India, the prevalence of hypothyroidism is strikingly high, with recent studies indicating that approximately 11% of the population is affected - a figure significantly higher than the global average[3]. While historically attributed to iodine deficiency, the sustained high prevalence despite successful iodization programs suggests a complex interplay of factors including genetic predisposition, environmental influences, and potentially autoimmune processes[4,5]. This persistent high prevalence in India underscores the urgent need for comprehensive research on the condition's multisystemic effects.

While the influence of thyroid hormone on the heart and skeletal muscles has been extensively explored[6,7], its effects on renal function remain underappreciated and, at times, overlooked in clinical practice. This oversight is particularly concerning in the Indian context, where the burden of both thyroid disorders and kidney diseases is substantial[1].

The kidney plays a vital role in maintaining homeostasis through its complex filtration, reabsorption, and secretion

processes, regulating fluid balance, electrolyte concentrations, and acid-base status[8]. Recent evidence suggests that thyroid hormones may act as silent orchestrators of renal physiology, influencing everything from glomerular filtration rate to electrolyte balance[9,10]. This revelation has opened up new avenues for understanding the multifaceted nature of hypothyroidism and its systemic effects, especially relevant in a country where hypothyroidism is increasingly recognized as a major public health concern[1].

Historically, the connection between thyroid dysfunction and kidney disease was primarily viewed through the lens of iodine metabolism[5]. However, emerging research hints at a more nuanced relationship, where thyroid hormones directly modulate renal blood flow, tubular function, and even the renin-angiotensin-aldosterone system. These findings challenge the traditional compartmentalized approach to organ systems and call for a more integrated view of endocrine-renal interactions, particularly in populations with a high prevalence of thyroid disorders[1,11].

The distinction between overt and subclinical hypothyroidism adds another layer of complexity to this relationship. While overt hypothyroidism presents with clear clinical symptoms and biochemical markers, subclinical hypothyroidism often lurks beneath the surface, its effects on various organ systems, including the kidneys, remaining elusive. This dichotomy raises important questions about the threshold at which thyroid dysfunction begins to impact renal function and the potential for early interventions, especially in a country like India where screening and early detection programs for thyroid disorders are still evolving.

This study seeks to bridge the gap in the current understanding of the thyroid-kidney relationship by systematically examining renal function parameters in both overt and subclinical hypothyroid patients. The aim is to elucidate the often-overlooked renal manifestations of thyroid dysfunction and contribute to more comprehensive care strategies. At the intersection of endocrinology and nephrology, this research may provide insights to reshape approaches to hypothyroidism management and renal health monitoring, particularly relevant in regions with high prevalence of thyroid disorders.

2.Materials and Methods

This prospective, observational cross-sectional study was conducted at Gandhi Medical College and Hamidia Hospital, Bhopal, from August 2022 to February 2024. The collaborative effort between the Departments of Medical Biochemistry and Medicine aimed to elucidate the renal implications of hypothyroidism. The study protocol adhered to the Declaration of Helsinki and received approval from the Institutional Ethics Committee (certificate no. 32228/MC/IEC/2022). All 150 participants provided written informed consent after a thorough explanation of the study procedures. Adults (>18 years) with recently diagnosed or suboptimally managed hypothyroidism attending the Medicine Outpatient Department were included, while those with pre-existing renal impairment, cardiovascular diseases, diagnosed autoimmune disorders, or using medications known to interfere with thyroid or renal function parameters were excluded.

The sample size was calculated using the formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

where z = 1.96 (95% confidence level), p = 11% (prevalence of hypothyroidism in India)[3], and d = 5% (desired precision). This yielded a minimum required sample of 150 participants. Venous blood samples (5 mL) were collected under aseptic conditions and processed according to the National Committee for Clinical Laboratory Standards guidelines[12]. Serum separation was achieved by centrifugation at 3000 rpm for 15 minutes. Thyroid function assessment (TSH, T3, and T4) was performed using Enzyme-Linked Immunosorbent Assay (ELISA) with a MicroLab ELISA Reader[13]. Renal function markers included serum creatinine (measured using the Jaffe-Compensated method on a Biosystem BA400 autoanalyzer), creatinine clearance (estimated using the Cockcroft-Gault equation), and microalbuminuria (assessed in spot urine samples using a dipstick Tetrabromophenol Blue reagent method)[14,15].

Participants were stratified into two cohorts based on their thyroid profiles: Group A with Overt Hypothyroidism (n=56) and Group B with Subclinical Hypothyroidism (n=94). Data analysis was performed using SPSS software (version 21.0, Chicago, SPSS Inc.). Normality of continuous variables was assessed using the Shapiro-Wilk test. Descriptive statistics, between-group comparisons, and correlation analyses were conducted using appropriate statistical tests. Multiple linear regression analysis was performed to identify independent predictors of renal function parameters, adjusting for potential confounders. A two-tailed p-value <0.05 was considered statistically significant for all analyses.

3.Results and Discussion

The present study, conducted on 150 hypothyroid patients, revealed significant alterations in renal function parameters associated with thyroid dysfunction. Patients were categorized into two groups: Group A with overt hypothyroidism (37.3%) and Group B with subclinical hypothyroidism (62.7%).

Serum creatinine levels, a key indicator of renal function, were significantly elevated in patients with overt hypothyroidism compared to those with subclinical hypothyroidism ($p<0.001$). In Group A, 85.7% of patients showed elevated creatinine levels (1.59 ± 0.21 mg/dL), while in Group B, 37.2% had elevated levels (1.21 ± 0.29 mg/dL).

These findings are consistent with several previous studies. Patil et al., 2018 found that serum creatinine levels were significantly higher in both overt and subclinical hypothyroid groups compared to euthyroid controls[16]. Similarly, Tayal et al., 2009 in their study, reported increased serum creatinine levels in both subclinical and overt hypothyroid groups compared to euthyroid subjects[9]. They noted a negative correlation between serum creatinine

and T3 & T4 levels in the overt hypothyroid group, while a positive correlation was found with TSH levels.

Present study revealed that creatinine clearance, an important indicator of glomerular filtration rate, was significantly affected in hypothyroid patients. In Group A, 76.8% of patients had decreased creatinine clearance (mean 71.57 ± 10.31 mL/min/1.73 m²), compared to 41.5% in Group B (mean 88.07 ± 17.47 mL/min/1.73 m²). This statistically significant difference ($p<0.001$) indicates more pronounced renal impairment in overt hypothyroidism. These findings align with studies by El-Eshmawy et al., 2013 and Tejomani M et al., 2019, who reported reduced creatinine clearance in hypothyroid patients[11,17].

Table 1: Distribution of Serum Creatinine level, Creatinine Clearance, and Microalbuminuria between study groups

Study Groups		Group A	Group B	p-value
No. of Cases		56 (37.3%)	94 (62.7%)	-
Serum Creatinine (mg/dL)	High (> 1.3)	48 (85.7%)	35 (37.2%)	<0.001*
	Mean ± SD	1.59 ± 0.21	1.21 ± 0.29	<0.001*
Creatinine Clearance (mL/min/1.73 m²)	Low (<90)	43 (76.8%)	39 (41.5%)	<0.001*
	Mean ± SD	71.57 ± 10.31	88.07 ± 17.47	<0.001*
Microalbuminuria		26 (46.4%)	31 (33.0%)	>0.05

[*Statistically Significant]

A significant positive correlation was observed between serum TSH and creatinine ($r=0.208$, $p=0.011$), while serum T_4 showed a strong negative correlation with creatinine ($r=-0.546$, $p<0.001$). These correlations underscore the direct influence of thyroid function on renal function. The relationship between TSH and creatinine suggests that as the severity of hypothyroidism increases (indicated by higher TSH levels), there is a corresponding increase in serum creatinine. Conversely, the negative correlation between T_4 and creatinine indicates that lower thyroid hormone levels are associated with higher creatinine levels, reflecting impaired renal function.

The present study also found that microalbuminuria, an early marker of renal dysfunction, was observed in 46.4% of patients with overt hypothyroidism (Group A) and 33.0% of patients with subclinical hypothyroidism (Group B). While this suggests a higher prevalence of microalbuminuria in overt hypothyroidism, the odds ratio analysis revealed interesting findings. For Group A, the odds ratio for microalbuminuria was 0.707 ($p > 0.05$), while for Group B, it was 1.246 ($p > 0.05$). Although these results were not statistically significant, they suggest a trend towards higher odds of microalbuminuria in subclinical hypothyroidism. These findings are supported by several previous studies. Parimoo et al., 2021 found a significant association between hypothyroidism and increased risk of microalbuminuria in a study of 100 patients[18]. Toda A et al., 2020 reported an independent association between subclinical hypothyroidism and higher prevalence of albuminuria in a large non-diabetic population[19]. Liamis G et al., 2017 identified subclinical hypothyroidism as an independent predictor of microalbuminuria, with a prevalence of 21% in their study[10]. Toto R et al., 2004 concluded that hypothyroidism leads to increased transcapillary leaking of plasma proteins, resulting in mild proteinuria and microalbuminuria[20]. While these studies generally support the association between hypothyroidism and microalbuminuria, the variation in findings, including our non-significant results, underscores the complex nature of this relationship and the need for further research.

The probable reasons for this decrease include hemodynamic changes such as reduced cardiac output and renal blood flow, direct effects of thyroid hormone deficiency on kidney structure and function, altered tubular function, and changes in muscle metabolism affecting creatinine production[1,8]. Tayal et al., 2009 observed that these decrements in renal function were reversible with thyroid hormone replacement, highlighting the dynamic nature of thyroid-kidney interactions[9]. The more severe impairment in overt hypothyroidism suggests a dose-dependent effect of thyroid hormone deficiency on renal function, emphasizing the importance of prompt treatment and regular monitoring of renal function in hypothyroid patients. Similarly, the study by Shin et al., 2012, which demonstrated that thyroid hormone deficiency can lead to a reversible reduction in GFR[8]. The authors also found that thyroid hormone replacement therapy could improve renal function in patients with subclinical hypothyroidism, highlighting the potential reversibility of renal impairment associated with hypothyroidism.

The impact of hypothyroidism on renal function extends beyond changes in serum creatinine. Although not directly measured in this study, previous research has shown that hypothyroidism can affect other aspects of kidney function, including alterations in electrolyte balance, particularly hyponatremia[10]. Furthermore, hypothyroidism has been associated with decreased renal ability to concentrate urine, potentially leading to mild fluid retention and edema[1].

These results highlight the complex interplay between thyroid function and renal physiology. The thyroid-kidney axis involves multiple mechanisms, including hemodynamic changes, alterations in metabolism, and potential effects on the renin-angiotensin-aldosterone system[1]. Understanding these interactions is crucial for the comprehensive management of patients with thyroid disorders.

4.Conclusion

This study demonstrates a significant effect of hypothyroidism on renal function, as evidenced by elevated serum creatinine levels and their correlation with thyroid function parameters. These findings emphasize the need for regular monitoring of renal function in hypothyroid patients, even in subclinical cases. Further research, particularly longitudinal studies, is needed to fully elucidate the long-term effects of hypothyroidism on kidney function and the

potential benefits of early thyroid hormone replacement therapy in preserving renal function.

5.Limitations of the Study

The present study had several limitations. Being a single-center study, it may have limited geographic and demographic diversity. The cross-sectional design of the study limited the ability to establish causal relationships between hypothyroidism and observed renal functional changes. Being a point-in-time study, the effect of thyroid hormone replacement therapy on renal parameters could not be assessed. Additionally, microalbuminuria was assessed qualitatively by dipstick method rather than quantitatively, potentially limiting the precision of this parameter. Future multi-centric, longitudinal studies incorporating quantitative microalbuminuria assessment would help overcome these limitations.

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